

AMENDMENTS TO THE SPECIFICATION:

At page 1, please delete the first full paragraph following the heading "Related Applications" and insert therefor:

This application is a continuation of U.S. Serial No. 08/312,914, filed September 30, 1994 (now abandoned), which is a continuation of U.S. Serial No. 08,137,745, filed October 19, 1993 (now abandoned), which is a continuation of U.S. Serial No. 08/015,390, filed February 8, 1993 (now abandoned), which is a continuation of U.S. Serial No. 07/670,242, filed March 15, 1991 (now abandoned), which is a continuation-in-part of U.S. Serial No. 07/659,974, filed February 22, 1991 (now abandoned), which is a continuation-in-part of U.S. Serial No. 07/537,305, filed June 11, 1990, (now abandoned) which is a continuation-in-part of U.S. Serial No. 07/497,098, filed March 20, 1990 (now abandoned), which is a continuation-in-part of U.S. Serial No. 07/444,669, filed December 1, 1989 (now abandoned), which is a continuation-in-part of U.S. Serial No. 06/937,793, filed December 4, 1986 (now abandoned), which is a continuation-in-part of U.S. Serial No. 06/819,314, filed January 16, 1986 (now abandoned), of which U.S. Serial No. 07/382,094, filed July 19, 1989, (now abandoned) is a continuation.

Please delete the paragraph spanning pp. 37-38 and replace it with the following amended paragraph.

Figure 13 shows FISH with fourteen Rb-1 lambda phage clones (Rb-1 probe) in normal and abnormal metaphase spreads and interphase nuclei. Panels A and B show two pairs of bright and specific hybridization signals on normal lymphocyte metaphase preparations in the mid-region of the q-arm of chromosome 13. Panel B

further shows cohybridization with a 13/21 centromeric probe. Panel C shows a digital image analysis of the mapping of the Rb-1 gene on a metaphase chromosome using both the Rb-1 probe and the 13/21 centromeric-specific repeat probe. Panel D shows two bright and specific hybridization domains in interphase nuclei of normal lymphocytes. Panel E shows cohybridization of the Rb-1 probe and a 13/21 centromeric-specific probe to metaphase spreads of a fibroblast cell line (GMO5877) derived from a sporadic retinoblastoma patient. Intact chromosome 13s show both Rb-1 and centromere signals; whereas chromosome 13s with a Rb-1 deletion are slightly shortened and hybridize only with the centromeric probe. Panel F shows a digital image analysis of the GM05887 cell line metaphase showing both the normal and shortened chromosome 13 and wherein cohybridization was effected with both the Rb-1 and 13/21 centromeric probe. Panel G shows hybridization of the Rb-1 probe to a aGM05887 cell line interphase. Panel H shows hybridization of the Rb-1 probe to a clinical breast cancer specimen. Panel I shows a digital image analysis of a dual color hybridization to a normal interphase nucleus; differently labeled ~~proteins~~ portions of the Rb-1 probe—a 3' (~~green~~) and a 5' (~~red~~) portion—were hybridized to the normal interphase nucleus.

Please replace the second full paragraph on page 39 with the following amended paragraph.

Figure 18 shows the simultaneous dual color hybridization with a chromosome 3 centromeric specific probe (~~green~~) and a chromosome 3 locus-specific cosmid probe mapped to 3p21 (~~red~~) to (A) metaphase spreads and (B) interphase nuclei of normal lymphocytes.

Please replace the paragraph which spans pp. 39-40 with the following amended paragraph.

Figure 19 shows hybridizations corresponding to those shown in Figure 18 wherein the metaphase spreads (A) and interphase nucleus (B) are from an ovarian cancer cell line (RMUG-S). In Panel A, the metaphase chromosome on the right exhibits an apparent 3p deletion whereas the metaphase chromosome on the left appears intact. In Panel B, chromosome 3 aneuploidy is demonstrated by the four green labeled centromeric domains; two intact chromosome 3s are indicated by two pairs of adjacent ~~green and red dots~~; and two 3p deleted chromosome 3s are indicated by the two single ~~green~~ labeled domains.

Please replace the first full paragraph on p. 40 with the following amended paragraph.

Figure 20 shows the simultaneous hybridizations of an AAF-labeled chromosome 3 centromere-specific probe (from H. Willard at Stanford) and a biotinylated chromosome 3q cosmid probe (J14R1A12; probes describe infra under Section X) to a metaphase spread and interphase nucleus of normal lymphocytes. A normal pattern is shown, ~~that is, two green and two pairs of red signals per cell.~~

Please replace the second full paragraph on p. 40 with the following amended paragraph.

Figure 21 shows hybridizations comparable to that shown in Figure 20 except that the interphase nucleus is from an ovarian cancer cell line (RMUG-S). An abnormal pattern is shown, that is, four chromosome 3 centromere-specific green

signals and four chromosome 3q cosmid ~~red~~ signals, indicating that the nucleus contains four long arms of chromosome 3.